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EXAMINER
FRONDA, CHRISTIAN L

ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,052	KIM ET AL.	
	Examiner	Art Unit	
	Christian L. Fronda	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 July 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/06, 02/07, 09/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-10 as listed in claim set of the preliminary amendment filed 07/31/2006 are pending and under consideration in this Office Action.

2. The information disclosure statements (IDS) submitted on 07/31/2006, 02/16/2007, and 09/10/2007 have been considered and a signed copy of form PTO-1449 for each IDS is enclosed with the instant Office Action.

3. Claims 1 and 2 are objected to for reciting the phrase "SEQ. ID. No.", which should be written as "SEQ ID NO". According to MPEP § 2422 sequences in the specification and claims must use a sequence identifier preceded by "SEQ ID NO".

Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 recites the phrase "*Escherichia coli* **DH5@/pRLSA** deposited with accession number of KCTC 10573BP"(emphasis added), which renders the claim vague and indefinite. This is because the instant specification discloses that *E. coli* BL21(DE3)pLysS transformed with

plasmid pRSET-LSA is accession number KCTC 10573BP and not *E. coli* DH5@/pRLSA (see page 7, lines 21-27; and page 12, lines 11-27) . The metes and bounds of the claim are uncertain since it is unclear if applicants actually intended to recite the *E. coli* BL21(DE3)pLysS transformed with pRSET-LSA as accession number KCTC 10573BP. Appropriate correction is requested.

For examination purposes it is assumed that *E. coli* BL21(DE3)pLysS transformed with plasmid pRSET-LSA is accession KCTC 10573BP, where plasmid pRSET-LSA contains a polynucleotide comprising the nucleotide sequence SEQ ID NO: 2 that encodes the protein comprising the amino acid sequence of SEQ ID NO: 1. Confirmation of this assumption is requested in response to the instant Office Action.

Claim Rejections - 35 U.S.C. § 101

6. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 1 and 2 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1 and 2 as written read on a products of nature. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor (see MPEP 2105). For example, amending the claims to recite "A purified protein…" or "An isolated gene…" would obviate this rejection (see the specification, for example, page 8, lines 21-24; and page 11, lines 4-5).

Claim Rejections - 35 U.S.C. § 112, First Paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-4 and 6-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated protein comprising the amino acid sequence of SEQ ID NO: 1 which has the activity of hydrolyzing amylopectin, starch glycogen and amylase; an isolated polynucleotide encoding said protein comprising the nucleotide sequence of SEQ ID NO: 2; a transformed prokaryotic or eukaryotic cell expressing said polynucleotide comprising the nucleotide sequence of SEQ ID NO: 2, a method for producing an enzyme having activity of hydrolyzing amylopectin, starch glycogen and amylase comprising culturing said transformed prokaryotic or eukaryotic cell expressing said polynucleotide comprising the nucleotide sequence of SEQ ID NO: 2; and a composition comprising said enzyme produced by said method , where said composition is used for dextran removal during sugar production, for plaque elimination, or as a mouth wash; **does not** reasonably provide enablement for any derivative or any fragment of a protein comprising an amino acid sequence of SEQ ID NO: 1, where the said derivative or fragment has any amino acid sequence and any biological activity; any gene of SEQ ID NO: 2; and any derivative or any fragment of a gene of SEQ ID NO: 2, where the said derivative or fragment has any nucleotide sequence and any biological activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

According to MPEP 2164.01(a), factors considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited

to: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

MPEP§ 2164.04 states that while the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection. The language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims. Accordingly, the factors most relevant to the instant rejection are addressed in detail below.

The breadth of the claims: Claim 1 encompasses any derivative or any fragment of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1, where the said derivative or fragment has any amino acid sequence and any biological activity. In absence of any specific definition for the term "derivative" from the instant specification, a "derivative" of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1 is broadly interpreted to be any protein of any biological function comprising an altered amino acid sequence having one or more amino acid modifications in SEQ ID NO: 1, where such modifications include amino acid substitution, addition, deletion, and combinations thereof. A "fragment" of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1 is broadly interpreted to be any protein of any biological function comprising any fragment of SEQ ID NO: 1.

Claim 2 encompasses any derivative or any fragment of the claimed gene of SEQ ID NO: 2, where the said derivative or fragment has any nucleotide sequence and any biological activity. In absence of any specific definition for the term "derivative" from the instant specification, a "derivative" of the claimed gene of SEQ ID NO: 2 is broadly interpreted to be any polynucleotide of any biological function comprising an altered nucleotide sequence having one or more

nucleotide modifications in SEQ ID NO: 2, where such modifications include nucleotide substitution, addition, deletion, and combinations thereof. A "fragment" of the claimed gene of SEQ ID NO: 2 is broadly interpreted to be any polynucleotide of any biological function comprising any fragment of SEQ ID NO: 2. Furthermore, gene elements which are not particularly described by the specification, including regulatory elements, introns, and untranslated regions, are essential to the function of the invention of claim 2 and are encompassed by claim 2 since the claim recites a "gene of SEQ ID NO: 2".

The state of the prior art; The relative skill of those in the art; and The predictability or unpredictability of the art: It is well known in the prior art that the amino acid sequence of a protein determines the protein's structural and functional properties. Predictability of which changes can be tolerated in a protein's amino acid sequence to obtain a desired biological activity requires knowledge and guidance regarding specific amino acid residue(s) in the protein's amino acid sequence, if any, are tolerant of modification and which are conserved (i.e., expectedly intolerant to modification) and detailed knowledge of the protein's structure, and the ways in which the protein's structure relates to its function. The reference of Chica et al. (Curr Opin Biotechnol. 2005 Aug;16(4):378-84; PTO 892) teaches that the complexity of the structure/function relationship in enzymes has proven to be the factor limiting the general application of rational enzyme modification and design, where rational enzyme modification and design requires in-depth understanding of structure/function relationships.

The positions within a protein's amino acid sequence where modifications can be made with a reasonable expectation of success in obtaining a protein having the same biological activity are limited in any protein and the result of such modifications is highly unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g., multiple substitutions, deletions, additions, and combinations thereof.

Methods for isolating or generating variants and mutants using random mutagenesis techniques were known in the art. However, neither the specification nor the state of the art at

the time of the invention provided the necessary guidance for altering the protein comprising an amino acid sequence of SEQ ID NO: 1 and its encoding gene of SEQ ID NO: 2 with an expectation of obtaining a protein derivative and its encoding gene derivative having the same biological activity. At the time of the invention, there was a high level of unpredictability associated with altering a protein sequence with an expectation that the protein will maintain the same desired biological activity. For example, the reference of Witkowski et al. (Biochemistry. 1999 Sep 7; 38(36): 11643-50; PTO 892) teaches that only a single amino acid substitution results in conversion of the activity of a protein to a second, distinct activity (see e.g., Table 1, page 11647). In addition, the reference of Seffernick et al. (J Bacteriol. 2001 Apr; 183 (8): 2405-10; PTO 892) teaches that two proteins with 98% amino acid sequence identity were found to catalyze different reactions, where one protein has melamine deaminase activity and the other protein has atrzine chlorohydrolase activity (see Fig.3, page 2408; **DISCUSSION** section on page 2409).

Gene elements which are not particularly described by the specification, including regulatory elements, introns, and untranslated regions, are essential to the function of the invention of claim 2 since the claim recites a "gene of SEQ ID NO: 2". Additionally, SEQ ID NO: 2 is disclosed as being essential to the function of the claimed invention since it encodes a protein comprising an amino acid sequence of SEQ ID NO: 1. The art indicates that the structure of genes which have regulatory elements, introns, and untranslated regions is empirically determined. For example, the structural elements of "gene" mediating the expression of a particular protein in the liver may be different than the structural elements of the "gene" mediating the expression of the same protein in the brain. Therefore, the structure of these elements which applicants considers as being essential to the function of the claim are not conventional in the art. The reference of Attwood (Science. 2000 Oct 20; 290: 471-473); PTO 892) teaches uncertainty in predicting the number of genes and their introns and exons in an organism, such as *Drosophila* and human, and uncertainty in the definition of "gene" because it is unclear if a "gene" encodes a protein or proteins or is translated or untranslated.

The amount of direction provided by the inventor; and The existence of working examples: The specification discloses one working example, which is an isolated protein from *Lipomyces starkeyi* KFCC-11077 comprising the amino acid sequence of SEQ ID NO: 1 that has dextranase and amylase activity and its encoding polynucleotide comprising the nucleotide sequence of SEQ ID NO: 2, where said isolate protein has the activity of hydrolyzing amylopectin, starch, glycogen, and amylase. However, the specification fails to disclose any specific guidance for altering the protein comprising the amino acid sequence of SEQ ID NO: 1 and its encoding gene of SEQ ID NO: 2 with the expectation that the protein will maintain the same biological activity. In particular, the specification fails to disclose any specific guidance for altering the protein comprising the amino acid sequence of SEQ ID NO: 1 and its encoding gene of SEQ ID NO: 2 with the expectation that the protein will still have dextranase and amylase activity, because guidance and working examples teaching unalterable structural and catalytic amino acid residues and amino acid residues tolerable to change is not provided by the specification.

The specification does not provide specific guidance regarding any biological function or any specific and substantial use for the claimed derivative or fragment of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1. The specification does not provide guidance regarding any specific biological function or any specific and substantial use for the claimed derivative or fragment of the claimed gene of SEQ ID NO: 2. Further, the term "A protein comprising an amino acid sequence of SEQ ID NO: 1" encompasses a full-length sequence as well as a fragment thereof because of "an".

There is no known or disclosed correlation between the coding region of a polynucleotide encoding the claimed protein comprising an amino acid sequence of SEQ ID NO: 1 and the structure of the non-described regulatory elements, introns, and untranslated regions of the "gene of SEQ ID NO: 2". The specification does not provide a specific guidance for regulatory elements, introns, and untranslated regions of the "gene of SEQ ID NO: 2" let alone any fragment or derivative thereof. Therefore, the specification does not provide specific guidance

for the claimed "gene of SEQ ID NO: 2".

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: While methods of isolating and/or generating variants of a protein were known in the art at the time of the invention and the specification provides general teachings for searching and screening for the claimed invention, it was not routine in the art to screen by a trial and error process for all proteins having a substantial number of modifications as encompassed by the claim(s) for those that maintain the same desired biological activity. It was not routine in the art to screen and search for a specific any specific biological function or any specific and substantial use for the claimed derivative or fragment of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1. It was not routine in the art to screen and search for a specific biological function or any specific and substantial use for the claimed derivative or fragment of the claimed gene of SEQ ID NO: 2.

Therefore, in view of the overly broad scope of the claims, the specification's lack of specific guidance and additional working examples, the high level of unpredictability as evidenced by the prior art, and the amount of experimentation required, it would require undue experimentation for a skilled artisan to make and use any derivative or any fragment of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1, where the said derivative or fragment has any amino acid sequence and any biological activity, and any derivative or any fragment of the claimed gene of SEQ ID NO: 2, where the said derivative or fragment has any nucleotide sequence and any biological activity

Such undue experimentation involves searching and screening a vast number of biological sources for any derivative of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1 and its encoding gene, and determine its biological function, where such derivative has an altered amino acid sequence having one or more amino acid modifications in SEQ ID NO: 1 (e.g., amino acid substitution, addition, deletion, and combinations thereof). Undue experimentation involves searching and screening a vast number of biological sources for any fragment of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1 and its

encoding gene with its regulatory elements, introns, and untranslated regions; and ascertaining its biological function.

Such undue experimentation also involves trial and error searching and screening for any one or more amino acids in SEQ ID NO: 1 to change (e.g., amino acid deletion, insertion, substitution, and combinations thereof) to thereby make a "derivative" of the claimed protein comprising the amino acid sequence of SEQ ID NO: 1, determining its biological function, and then searching for and/or synthesizing the polynucleotide encoding this protein "derivative". Undue experimentation involves searching and screening a vast number for any fragment of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1 and its encoding gene with its regulatory elements, introns, and untranslated regions; and ascertaining its biological function.

General teachings from the specification regarding screening and searching for the claimed invention is not specific guidance for making and using the claimed invention.

Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988).

Dependent claims 3, 4, and 6-10 are included in the rejection because these claims do not correct the defect of claims 1 or 2.

10. Claim 5 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the recited *Escherichia coli* deposited with accession number KCTC

10573BP recited in claim 5 is required to practice the claimed invention. As such the said *Escherichia coli* of accession number KCTC 10573BP must be readily available or obtainable by a repeatable method stated in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the requirements of 35 USC § 112, first paragraph, may be satisfied by a deposit of the *Escherichia coli* of accession number KCTC 10573BP. See 37 CFR 1.801-1.809.

The process disclosed in the specification to make the said *Escherichia coli* of accession number KCTC 10573BP does not appear to be repeatable. The nucleotide sequence of the plasmid pRSET-LSA is not fully disclosed, nor have all the nucleotide sequences required for its construction been shown to be biblically known and freely available. The specification does not disclose a repeatable process to obtain the said *Escherichia coli* of accession number KCTC 10573BP and it is not apparent if the nucleotide sequences to make the plasmid pRSET-LSA are readily available to the public. It is not apparent if the source materials to make the said *Escherichia coli* deposited with accession number KCTC 10573BP recited in claim are both known and readily available to the public.

Applicants' referral to deposit number KCTC 10573BP is noted but is considered insufficient assurance that all of the conditions of 37 CFR 1.801-1.809 have been met since there is no indication in the specification as to its public availability.

If the deposit has been made under the terms of the Budapest Treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the said *Escherichia coli* deposited with accession number KCTC 10573BP has been deposited under the Budapest Treaty and that the said *Escherichia coli* deposited with accession number KCTC 10573BP will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808.

If the deposit has not been made under the Budapest Treaty, then an affidavit or

declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature must be made, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met.

Amendment of the specification to recite the date of deposit for the said *Escherichia coli* of accession number KCTC 10573BP and the complete name and address of the depository is required.

11. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

According to MPEP 2163, to satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba, B.V. v.Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed.Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116.

Claim 1 is drawn to any derivative or any fragment of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1, where the said derivative or fragment has any amino acid sequence and any biological activity. Claim 2 is drawn to any derivative or any fragment of the claimed gene of SEQ ID NO: 2, where the said derivative or fragment has any nucleotide sequence and any biological activity. The derivative or fragment recited in claims 1 and 2 do not recite any particular and specific structure to function relationship. The claims do not require that the derivatives or fragments possess any particular biological activity, any particular conserved structure, or any other distinguishing feature

Therefore, claim 1 is drawn to a genus of derivatives or fragments of the claimed protein

comprising an amino acid sequence of SEQ ID NO: 1, where the said derivatives or fragments have any amino acid sequence and any biological activity. Claim 2 is drawn to a genus of derivatives or fragments of the claimed gene of SEQ ID NO: 2, where the said derivatives or fragments have any nucleotide sequence and any biological activity.

The scope of the each genus includes many members with widely differing structural, chemical, and physiochemical properties such as widely differing amino acid sequences, nucleotide sequences, and biological functions. Furthermore, each genus is highly variable because a significant number of structural and biological differences between genus members exist.

For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

The instant specification discloses only one isolated protein comprising the amino acid sequence of SEQ ID NO: 1 and only one isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO: 2 which encodes said isolated protein comprising the amino acid sequence of SEQ ID NO: 1. The instant specification discloses that the isolated protein comprising the amino acid sequence of SEQ ID NO: 1 has dextranase and amylase activities.

However, the instant specification does not describe and define any structural features, amino acid sequences, nucleotide sequences, and/or biological functions that are commonly possessed by members of each claimed genus. The specification does not describe any biological function for the claimed derivative or fragment of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1. The specification does not describe any specific biological function

for the claimed derivative or fragment of the claimed gene of SEQ ID NO: 2.

The specification fails to disclose a representative number of species of each claimed genus, which includes many members with widely differing structural, chemical, and biological functions. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the isolated protein comprising the amino acid sequence of SEQ ID NO: 1 is insufficient to be representative of the attributes and features common to all the members of the claimed genus of derivatives or fragments of the claimed protein comprising an amino acid sequence of SEQ ID NO: 1, where the said derivatives or fragments have any amino acid sequence and any biological activity. Furthermore, the isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO: 2 is insufficient to be representative of the attributes and features common to all the members of the claimed genus of derivatives or fragments of the claimed gene of SEQ ID NO: 2, where the said derivatives or fragments have any nucleotide sequence and any biological activity. Thus, one skilled in the art cannot visualize or recognize the identity of members of each claimed genus.

Furthermore, gene elements which are not particularly described by the specification, including regulatory elements, introns, and untranslated regions, are essential to the function of the invention of claim 2 since the claim recites a "gene of SEQ ID NO: 2". Additionally, SEQ ID NO: 2 is disclosed as being essential to the function of the claimed invention since it encodes a protein comprising an amino acid sequence of SEQ ID NO: 1. The art indicates that the structure of genes encompassing regulatory elements, introns, and untranslated regions is empirically determined. For example, the structural elements of "gene" mediating the expression of a particular protein in the liver may be different than the structural elements of the "gene" mediating the expression of the same protein in the brain. Therefore, the structure of these elements which applicants considers as being essential to the function of the claim are not conventional in the art.

There is no known or disclosed correlation between the coding region of a polynucleotide encoding the claimed protein comprising an amino acid sequence of SEQ ID NO: 1 and the structure of the non-described regulatory elements, introns, and untranslated regions of the "gene of SEQ ID NO: 2". The specification does not provide a complete detailed description of regulatory elements, introns, and untranslated regions of the "gene of SEQ ID NO: 2" let alone any fragment or derivative thereof. Therefore, the specification does not provide a written description of the claimed "gene of SEQ ID NO: 2".

Vas-Cath, Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class, where the specification provided only the bovine sequence.

In view of the above considerations, one of skill in the art would not recognize that applicants were in possession of a genus of derivatives or fragments of a protein comprising an amino acid sequence of SEQ ID NO: 1, where the said derivatives or fragments have any amino acid sequence and any biological activity; a genus of derivatives or fragments of a gene of SEQ ID NO: 2, where the said derivatives or fragments have any nucleotide sequence and any biological activity; and a "gene of SEQ ID NO: 2". Therefore, only an isolated protein comprising the amino acid sequence of SEQ ID NO: 1 and an isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO: 2 meet the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. § 112, first paragraph, is severable from its enablement provision (see page 115).

Dependent claims 3 and 4 are included in the rejection because these claims do not correct the defect of claim 2. It is noted that claims 6-10 are not included in this rejection because claims 6-10 as written do recite a particular structure to function relationship.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:.

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1 and 7-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Kim et al. (US Patent 6,485,953, published 11/26/2002; PTO 892).

Kim et al. teach an isolated enzyme named DXAMase obtained from *Lipomyces starkeyi* KFCC-11077 (*L. starkeyi* KSM 22), which has dextranase and amylase activities and a molecular weight of 60 kilo Daltons on SDS-PAGE. Because the disclosed protein comprising an amino acid sequence of SEQ ID NO: 1 and the reference DXAMase are both obtained from the same source *Lipomyces starkeyi* KFCC-11077, have the same disclosed dextranase and amylase activities, and have about the same molecular weight; then in absence of facts to the contrary, the reference DXAMase inherently has the same amino acid sequence of SEQ ID NO: 1 and has the same activity as the claimed protein, such as hydrolyzing amylopectin, starch, glycogen, and amylase. See entire patent, especially claim 1; column 2, line 8 to column 3, line 18; column 4, lines 17-52; column 5, line 14 to column 10, line 12, in particular.

Claims 7-10 which are product-by-process claims are included in the rejection because according to MPEP § 2113:

> "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed.Cir. 1985) (citations omitted)"

Kim et al. teach a mouthwash composition comprising the reference DXAMase, which is used for plaque elimination. See entire patent, especially claim 1; column 2, lines 24-40; column 7, line 60 to column 10, line 12, in particular.

Kim et al. teach that the DXAMase having a molecular weight of 60 kilo Daltons is obtained from *Lipomyces starkeyi* KFCC-11077 (*L. starkeyi* KSM 22) using gel permeation chromatography, where an eluted fraction containing citrate phosphate buffer solution and the DXAMase having dextranase and amylase activities was collected. See column 4, lines 34-53.

Claim 9 is included in the rejection because a product is a product, irrespective of its intended use. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

14. Claims 1-4 and 6-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Steyn et al. (Gene. 1995 Dec 1;166(1):65-71; PTO 892). Because claim 1 recites "an amino acid sequence" of SEQ ID NO: 1, then the claim encompasses any protein comprising any fragment of SEQ ID NO: 1 as well as the full length sequence of SEQ ID NO: 1.

Steyn et al. teach an isolated starch-hydrolyzing α-amylase from *Lipomyces konoenkoae* (Accession Q01117) comprising "an amino acid sequence" of SEQ ID NO: 1 of the instant application, wherein said isolated α-amylase comprises an amino acid sequence that is 88.4% identical to SEQ ID NO: 1. The reference α-amylase has the property of liberating reducing

groups from glucose polymers containing both α-1,4 and α-1,6 bonds. See entire reference publication, especially page 66, right column, lines 19-22; page 68, left column, first paragraph, line 1 to page 70, left column, line 8; Fig. 3 on page 68; and Fig 5 on page 70. See below the alignment of the amino acid sequence of the reference α-amylase to SEQ ID NO: 1 of the instant application.

Alignment of Accession Q01117 of Steyn et al. and SEQ ID NO: 1 of instant application

```
ID   AMY1_LIPKO     STANDARD;      PRT;   624 AA.
AC   Q01117;
DT   19-SEP-2003, integrated into UniProtKB/Swiss-Prot.
DT   01-NOV-1998, sequence version 2.
DT   30-MAY-2006, entry version 43.
DE   Alpha-amylase 1 precursor (EC 3.2.1.1) (1,4-alpha-D-glucan
DE   glucanohydrolase 1).
GN   Name=LKA1;
OS   Lipomyces kononenkoae.
OC   Eukaryota; Fungi; Ascomycota; Saccharomycotina; Saccharomycetes;
OC   Saccharomycetales; Lipomycetaceae; Lipomyces.
OX   NCBI_TaxID=34357;
RN   [1]
RP   NUCLEOTIDE SEQUENCE [MRNA].
RC   STRAIN=IGC4052B;
RX   MEDLINE=96105202; PubMed=8529895; DOI=10.1016/0378-1119(95)00633-0;
RA   Steyn A.J.C., Marmur J., Pretorius I.S.;
RT   "Cloning, sequence analysis and expression in yeasts of a cDNA
RT   containing a Lipomyces kononenkoae alpha-amylase-encoding gene.";
RL   Gene 166:65-71(1995).
RN   [2]
RP   PROTEIN SEQUENCE OF 29-44.
RC   STRAIN=IGC4052B;
RX   MEDLINE=96132108; PubMed=8593683;
RA   Steyn A.J.C., Pretorius I.S.;
RT   "Characterization of a novel alpha-amylase from Lipomyces kononenkoae
RT   and expression of its gene (LKA1) in Saccharomyces cerevisiae.";
RL   Curr. Genet. 28:526-533(1995).
CC   -!- CATALYTIC ACTIVITY: Endohydrolysis of 1,4-alpha-D-glucosidic
CC       linkages in oligosaccharides and polysaccharides.
CC   -!- COFACTOR: Binds 2 calcium ions per subunit. Calcium is inhibitory
CC       at high concentrations (By similarity).
CC   -!- SUBCELLULAR LOCATION: Secreted protein.
CC   -!- SIMILARITY: Belongs to the glycosyl hydrolase 13 family.
CC   -!- SIMILARITY: Contains 1 CBM21 (carbohydrate binding type-21)
CC       domain.
CC   ---------------------------------------------------------------------
CC   Copyrighted by the UniProt Consortium, see http://www.uniprot.org/terms
CC   Distributed under the Creative Commons Attribution-NoDerivs License
CC   ---------------------------------------------------------------------
DR   EMBL; U30376; AAC49622.1; ALT_INIT; mRNA.
DR   PIR; JC4510; JC4510.
DR   HSSP; P10529; 7TAA.
DR   InterPro; IPR005036; CBM_21.
DR   InterPro; IPR006047; Glyco_hydro_13_cat.
DR   InterPro; IPR006589; Glyco_hydro_13_sub_cat.
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DR   Pfam; PF00128; Alpha-amylase; 1.
DR   Pfam; PF03370; CBM_21; 1.
DR   SMART; SM00642; Aamy; 1.
DR   PROSITE; PS51159; CBM21; 1.
KW   Calcium; Carbohydrate metabolism; Direct protein sequencing;
KW   Glycoprotein; Glycosidase; Hydrolase; Metal-binding; Signal.
FT   SIGNAL        1     28
FT   CHAIN        29    624       Alpha-amylase 1.
FT                                 /FTId=PRO_0000001354.
FT   DOMAIN       40    133       CBM21.
FT   ACT_SITE    353    353       Nucleophile (By similarity).
FT   ACT_SITE    377    377       Proton donor (By similarity).
FT   ACT_SITE    444    444       By similarity.
FT   METAL       268    268       Calcium 1 (By similarity).
FT   METAL       309    309       Calcium 1 (via carbonyl oxygen) (By
FT                                 similarity).
FT   METAL       322    322       Calcium 1 (By similarity).
FT   METAL       353    353       Calcium 2 (By similarity).
FT   METAL       357    357       Calcium 1 (via carbonyl oxygen) (By
FT                                 similarity).
FT   METAL       377    377       Calcium 2 (By similarity).
FT   CARBOHYD    304    304       N-linked (GlcNAc. . .) (Potential).
FT   CARBOHYD    344    344       N-linked (GlcNAc. . .) (Potential).
FT   DISULFID    177    185       By similarity.
FT   DISULFID    297    311       By similarity.
FT   DISULFID    387    430       By similarity.
FT   DISULFID    587    622       By similarity.
SQ   SEQUENCE   624 AA;  68877 MW;  87EB16534F5A9A9F CRC64;

  Query Match             88.4%;  Score 2981.5;  DB 1;  Length 624;
  Best Local Similarity   86.9%;  Pred. No. 7.5e-175;
  Matches  562;  Conservative   31;  Mismatches   31;  Indels   23;  Gaps    1;

Qy          1 MLLINFFIAVLGVISLSPIVVARYILRRDCTTVTVLSSPESVTSSNHVELASHEMCDSTL 60
              ||||||||||||||||||||||||||||||||||||||||||| ||||:|||:||| |||
Db          1 MLLINFFIAVLGVISLSPIVVARYILRRDCTTVTVLSSPESVTGSNHVQLASYEMCGSTL 60

Qy         61 SASLYIYNDDYDKIVTLYYLTSSGTTGSVTASYSSSLSNNWELWSLSAPAADAVEITGAS 120
              |||||:||||||||||||||||||||  |      |||||||:||| || ||||||||
Db         61 SASLYVYNDDYDKIVTLYYLTSSGTTGSTLALILPVWSNNWELWTLSAIAAGAVEITGAS 120

Qy        121 YVDSDASATYATSFDIPLTTTTTSSSSASATSTSSLTTTSSVSISVSVPTGTAANWRGRA 180
              |||||  |  ||  ||  |:|||||                        | ||||||||||||:
Db        121 YVDSDTSVTYTTSLDLPLTTT----------------------SASVPTGTAANWRGRS 157

Qy        181 IYEIVTDRFARTDGSTTYLCDVTDRVYCGGSYEGIINMLDYIEGMGFTAIWISPIVENIP 240
              ||::|||||||||| ||  |||||||||||| |||||||||:||||||||||||||||||
Db        158 IYQVVTDRFARTDGSITYSCDVTDRVYCGGSYRGIINMLDYIQGMGFTAIWISPIVENIP 217

Qy        241 DDTGYGYAYHGYWMKDIFALNTNFGTADDLIALATELHNRGMYLMVDIVVNHFAFSGSHA 300
              |||||||||||||||||||||||| |||||||||||||||||||||||||||||||:||
Db        218 DDTGYGYAYHGYWMKDIFALNTNFGGADDLIALATELHNRGMYLMVDIVVNHFAFSGNHA 277

Qy        301 DVDYSEYFPYSSEDYFHSFCWITDYSNETNVEQCWLGDDTVPLVDVNTELDTVKSEYQSW 360
              ||||||||||||:|||||||||||||:||||:||||||:|||||||:||||||||||||
Db        278 DVDYSEYFPYSSQDYFHSFCWITDYSNQTNVEECWLGDDSVPLVDVNTQLDTVKSEYQSW 337

Qy        361 VEELIANYSIDGLRIDTVKHVEMDFWAPFEEAAGIYAVGEVFDGDPSYTCPYEENLDGVL 420
              |::|||||||||||||||:|||||:|||||| ||||||||||||||:|||||||
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Db        338 VKQLIANYSIDGLRIDTVKHVQMDFWAPFQEAAGIYTVGEVFDGDPSYTCPYQENLDGVL 397

Qy        421 NYPVYYPVVSAFESVSGSVSSLVDMIDTLKSECTDTTLLGSFLENEDNPRFPSYTSDESL 480
              |||||||||||||: | ||:|||||||||||||| ||||||||||:|||||||||||||
Db        398 NYPVYYPVVSAFQRVGGSISSLVDMIDTLKSECIDTTLLGSFLENQDNPRFPSYTSDESL 457

Qy        481 IKNAIAFTMLSDGIPIIYYGEEQGLNGGNDPYNREALWLTGYSTTSTFYKYIASLNEIRN 540
              ||||||||:|||||||||:|||||||||||||||||| ||||||||||:|||||:|||
Db        458 IKNAIAFTILSDGIPIIYYGQEQGLNGGNDPYNREALWPTGYSTTSTFYEYIASLNQIRN 517

Qy        541 EAIYKDDTYLTYENWVIYSDSTTIAMRKGFTGNEIITVLSNLGTSGSSYTLTLSNTGYTA 600
               ||| |||||||:||||||||||||||||||:|||||||:|||||||||||||||||||
Db        518 HAIYIDDTYLTYQNWVIYSDSTTIAMRKGFTGNQIITVLSNLGSSGSSYTLTLSNTGYTA 577

Qy        601 SSVVYEILTCTAVTVDSSGNLAVPMSSGLPKVFYEESQLVGSGICSM 647
              |||||||||||||||| ||||||||| |||:||| ||||||||||||
Db        578 SSVVYEILTCTAVTVDLSGNLAVPMSGGLPRVFYPESQLVGSGICSM 624
```

Because the reference α-amylase and the claimed protein comprising an amino acid sequence of SEQ ID NO: 1 is isolated from the same genus *Lipomyces,* the reference α-amylase and the claimed protein comprising an amino acid sequence of SEQ ID NO: 1 both have α-amylase activity, the reference α-amylase and the claimed protein have approximately the same molecular weight based on the number of amino acids in their amino acid sequences, and the amino acid sequence of the reference α-amylase has a high sequence identity to SEQ ID NO: 1 of the instant application, then in absence of facts to the contrary the reference α-amylase inherently has the same activity as the claimed protein, such as having dextranase activity, amylase activity, and hydrolyzing amylopectin, starch, glycogen, and amylase. Since the reference α-amylase comprises "an amino acid sequence" of SEQ ID NO: 1 and has a high sequence identity to SEQ ID NO: 1 of the instant application, the reference α-amylase is also deemed to be a "derivative" of the claimed protein.

Steyn et al. teach an isolated cDNA fragment containing the LKA1 gene encoding the reference α-amylase from *Lipomyces konoenkoae* (Accession U30376), which has 78.2% identity with the claimed gene of SEQ ID NO: 2. See entire reference publication, especially page 66, left column, section titled **(a) Cloning of the *LKA1* gene** to page 69, left column, line 17; Fig 2; and Fig. 3, in particular. See below the alignment of Accession U30376 encoding the reference

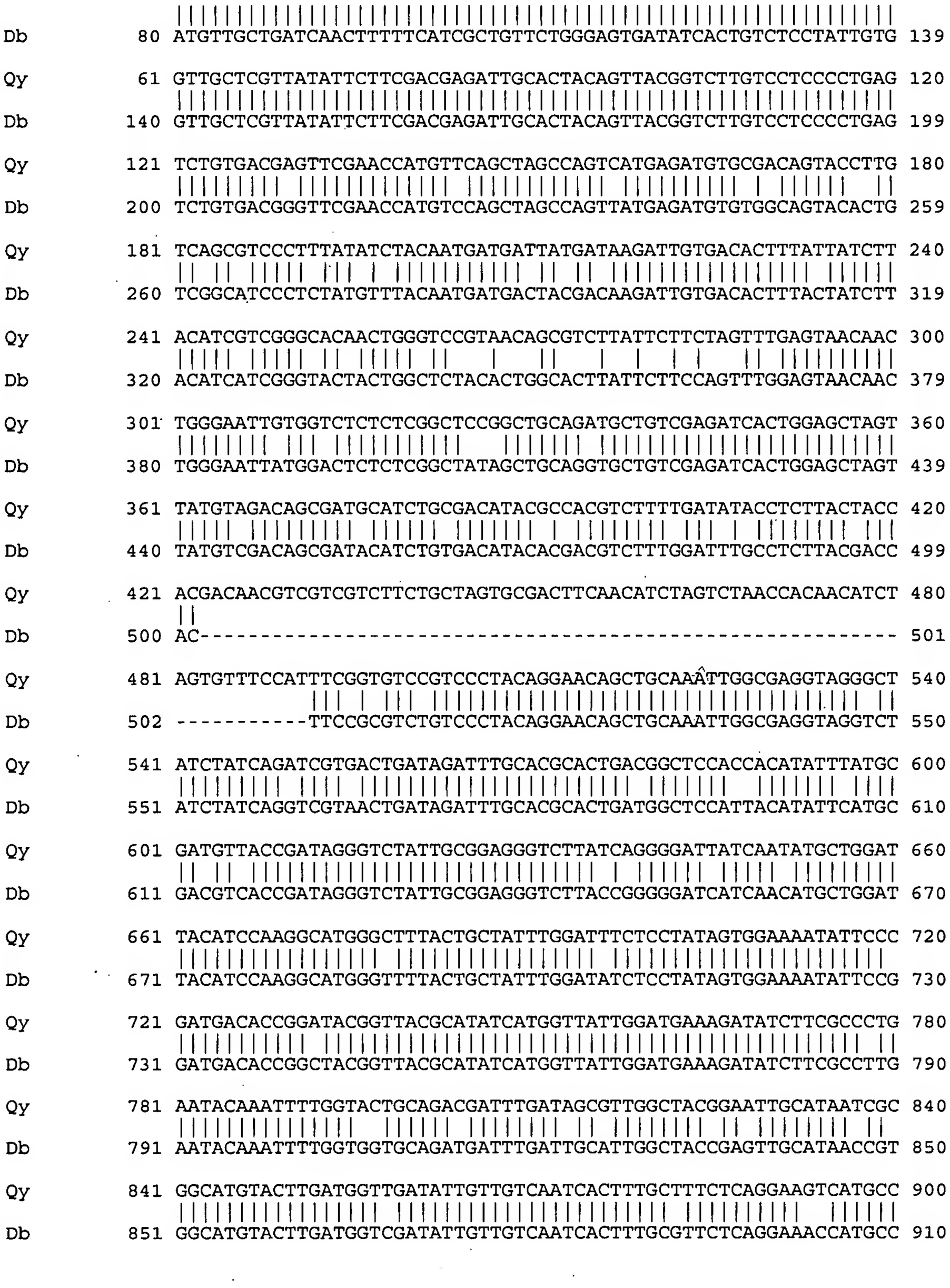
α-amylase to SEQ ID NO: 2 of the instant application.

Alignment of Accession U30376 of Steyn et al. and SEQ ID NO: 2 of instant application

```
RESULT 2
LKU30376
LOCUS       LKU30376                2239 bp    mRNA    linear   PLN 27-JAN-1997
DEFINITION  Lipomyces kononenkoae subsp. spencermartinsiae alpha-amylase mRNA,
            complete cds.
ACCESSION   U30376
VERSION     U30376.1  GI:1173536
KEYWORDS    .
SOURCE      Lipomyces spencermartinsiae
  ORGANISM  Lipomyces spencermartinsiae
            Eukaryota; Fungi; Ascomycota; Saccharomycotina; Saccharomycetes;
            Saccharomycetales; Lipomycetaceae; Lipomyces.
REFERENCE   1  (sites)
  AUTHORS   Steyn,A.J., Marmur,J. and Pretorius,I.S.
  TITLE     Cloning, sequence analysis and expression in yeasts of a cDNA
            containing a Lipomyces kononenkoae alpha-amylase-encoding gene
  JOURNAL   Gene 166 (1), 65-71 (1995)
   PUBMED   8529895
REFERENCE   2  (bases 1 to 2239)
  AUTHORS   Pretorius,I.S.
  TITLE     Direct Submission
  JOURNAL   Submitted (27-JUN-1995) Isak S. Pretorius, Microbiology, University
            of Stellenbosch, Victoria, Stellenbosch, Western Cape 7600, South
            Africa
FEATURES             Location/Qualifiers
     source          1. .2239
                     /organism="Lipomyces spencermartinsiae"
                     /mol_type="mRNA"
                     /strain="IGC4052B"
                     /sub_species="spencermartinsiae"
                     /db_xref="taxon:56873"
                     /lab_host="Saccharomyces cerevisiae"
     CDS             242. .1954
                     /codon_start=1
                     /product="alpha-amylase"
                     /protein_id="AAC49622.1"
                     /db_xref="GI:1173537"
                     /translation="MCGSTLSASLYVYNDDYDKIVTLYYLTSSGTTGSTLALILPVWS
                     NNWELWTLSAIAAGAVEITGASYVDSDTSVTYTTSLDLPLTTTSASVPTGTAANWRGR
                     SIYQVVTDRFARTDGSITYSCDVTDRVYCGGSYRGIINMLDYIQGMGFTAIWISPIVE
                     NIPDDTGYGYAYHGYWMKDIFALNTNFGGADDLIALATELHNRGMYLMVDIVVNHFAF
                     SGNHADVDYSEYFPYSSQDYFHSFCWITDYSNQTNVEECWLGDDSVPLVDVNTQLDTV
                     KSEYQSWVKQLIANYSIDGLRIDTVKHVQMDFWAPFQEAAGIYTVGEVFDGDPSYTCP
                     YQENLDGVLNYPVYYPVVSAFQRVGGSISSLVDMIDTLKSECIDTTLLGSFLENQDNP
                     RFPSYTSDESLIKNAIAFTILSDGIPIIYYGQEQGLNGGNDPYNREALWPTGYSTTST
                     FYEYIASLNQIRNHAIYIDDTYLTYQNWVIYSDSTTIAMRKGFTGNQIITVLSNLGSS
                     GSSYTLTLSNTGYTASSVVYEILTCTAVTVDLSGNLAVPMSGGLPRVFYPESQLVGSG
                     ICSM"
ORIGIN

  Query Match           78.2%;  Score 1521.2;  DB 4;  Length 2239;
  Best Local Similarity 87.6%;  Pred. No. 0;
  Matches 1704;  Conservative    0;  Mismatches  173;  Indels   69;  Gaps    1;

Qy          1 ATGTTGCTGATCAACTTTTTCATCGCTGTTCTGGGAGTGATATCACTGTCTCCTATTGTG 60
```


Db 80 ATGTTGCTGATCAACTTTTTCATCGCTGTTCTGGGAGTGATATCACTGTCTCCTATTGTG 139
Qy 61 GTTGCTCGTTATATTCTTCGACGAGATTGCACTACAGTTACGGTCTTGTCCTCCCCTGAG 120
Db 140 GTTGCTCGTTATATTCTTCGACGAGATTGCACTACAGTTACGGTCTTGTCCTCCCCTGAG 199
Qy 121 TCTGTGACGAGTTCGAACCATGTTCAGCTAGCCAGTCATGAGATGTGCGACAGTACCTTG 180
Db 200 TCTGTGACGGGTTCGAACCATGTCCAGCTAGCCAGTTATGAGATGTGTGGCAGTACACTG 259
Qy 181 TCAGCGTCCCTTTATATCTACAATGATGATTATGATAAGATTGTGACACTTTATTATCTT 240
Db 260 TCGGCATCCCTCTATGTTTACAATGATGACTACGACAAGATTGTGACACTTTACTATCTT 319
Qy 241 ACATCGTCGGGCACAACTGGGTCCGTAACAGCGTCTTATTCTTCTAGTTTGAGTAACAAC 300
Db 320 ACATCATCGGGTACTACTGGCTCTACACTGGCACTTATTCTTCCAGTTTGGAGTAACAAC 379
Qy 301 TGGGAATTGTGGTCTCTCTCGGCTCCGGCTGCAGATGCTGTCGAGATCACTGGAGCTAGT 360
Db 380 TGGGAATTATGGACTCTCTCGGCTATAGCTGCAGGTGCTGTCGAGATCACTGGAGCTAGT 439
Qy 361 TATGTAGACAGCGATGCATCTGCGACATACGCCACGTCTTTTGATATACCTCTTACTACC 420
Db 440 TATGTCGACAGCGATACATCTGTGACATACACGACGTCTTTGGATTTGCCTCTTACGACC 499
Qy 421 ACGACAACGTCGTCGTCTTCTGCTAGTGCGACTTCAACATCTAGTCTAACCACAACATCT 480
Db 500 AC 501
Qy 481 AGTGTTTCCATTTCGGTGTCCGTCCCTACAGGAACAGCTGCAAATTGGCGAGGTAGGGCT 540
Db 502 TTCCGCGTCTGTCCCTACAGGAACAGCTGCAAATTGGCGAGGTAGGTCT 550
Qy 541 ATCTATCAGATCGTGACTGATAGATTTGCACGCACTGACGGCTCCACCACATATTTATGC 600
Db 551 ATCTATCAGGTCGTAACTGATAGATTTGCACGCACTGATGGCTCCATTACATATTCATGC 610
Qy 601 GATGTTACCGATAGGGTCTATTGCGGAGGGTCTTATCAGGGGATTATCAATATGCTGGAT 660
Db 611 GACGTCACCGATAGGGTCTATTGCGGAGGGTCTTACCGGGGGATCATCAACATGCTGGAT 670
Qy 661 TACATCCAAGGCATGGGCTTTACTGCTATTTGGATTTCTCCTATAGTGGAAAATATTCCC 720
Db 671 TACATCCAAGGCATGGGTTTTACTGCTATTTGGATATCTCCTATAGTGGAAAATATTCCG 730
Qy 721 GATGACACCGGATACGGTTACGCATATCATGGTTATTGGATGAAAGATATCTTCGCCCTG 780
Db 731 GATGACACCGGCTACGGTTACGCATATCATGGTTATTGGATGAAAGATATCTTCGCCTTG 790
Qy 781 AATACAAATTTTGGTACTGCAGACGATTTGATAGCGTTGGCTACGGAATTGCATAATCGC 840
Db 791 AATACAAATTTTGGTGGTGCAGATGATTTGATTGCATTGGCTACCGAGTTGCATAACCGT 850
Qy 841 GGCATGTACTTGATGGTTGATATTGTTGTCAATCACTTTGCTTTCTCAGGAAGTCATGCC 900
Db 851 GGCATGTACTTGATGGTCGATATTGTTGTCAATCACTTTGCGTTCTCAGGAAACCATGCC 910

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Qy        901 GACGTGGACTACTCTGAATATTTCCCGTATTCGTCCCAGGATTATTTTCATTCATTTTGC 960
              |||||  ||  |||||||||||||||||  ||||||||  ||||||||||||||||||||||||
Db        911 GACGTCGATTACTCTGAATATTTCCCATATTCGTCTCAGGATTATTTTCATTCATTTTGC 970

Qy        961 TGGATTACAGATTACTCGAATCAGACAAACGTTGAGCAGTGCTGGCTTGGCGACGATACT 1020
              ||||||||  ||||||||  |||||  ||||||||||||  ||||||||||  ||||||||   ||
Db        971 TGGATTACGGATTACTCAAATCAAACAAACGTTGAGGAGTGCTGGCTCGGCGACGACTCT 1030

Qy       1021 GTTCCTCTCGTGGACGTCAATACCCAACTTGACACCGTGAAAAGTGAATATCAATCCTGG 1080
              ||||||||||||||||  |||||  ||||||||||||||||||||||||||||  ||||||
Db       1031 GTTCCTCTCGTGGACGTTAATACACAACTTGACACCGTGAAAAGTGAATATCAGTCCTGG 1090

Qy       1081 GTTCAAGAACTTATAGCTAATTACTCTATTGACGGCCTAAGAATTGACACCGTCAAGCAC 1140
              |||  ||  ||||||||||||||||||||||||  ||  ||  ||||||||||  ||||||||
Db       1091 GTTAAACAACTTATAGCTAATTACTCTATTGATGGTCTGAGAATTGACACTGTCAAGCAT 1150

Qy       1141 GTGCAGATGGATTTTTGGGCACCATTTCAAGAGGCTGCAGGGATTTACGCCGTTGGTGAA 1200
              ||||||||||||||||||||  ||||||||||||||  ||||||||||||  |  |||||||||
Db       1151 GTGCAGATGGATTTTTGGGCGCCATTTCAAGAGGCAGCAGGGATTTACACTGTTGGTGAA 1210

Qy       1201 GTATTCGACGGTGATCCATCCTACACATGTCCATATCAGGAAAATCTTGACGGTGTCTTG 1260
              ||||||||  ||||||||||||||  ||||||||  |||||  ||||||||  ||||||||  |||
Db       1211 GTATTCGATGGTGATCCATCCTATACATGTCCGTATCAAGAAAATCTCGACGGTGTTTTG 1270

Qy       1261 AATTATCCTGTTTATTATCCTGTCGTCTCTGCGTTTGAGAGTGTTAGTGGGTCGGTCTCC 1320
              ||||||||  ||||||||||||||  ||||||||  |||  ||  |||||  ||||||||  |  |||
Db       1271 AATTATCCCGTTTATTATCCTGTTGTCTCTGCTTTTCAGCGTGTTGGTGGGTCGATATCC 1330

Qy       1321 TCGTTAGTCGATATGATTGATACGCTCAAGTCTGAATGCACCGACACTACTCTCCTAGGC 1380
              ||||||||||||||||||||||||||||||||||||||||  ||||||||||||||||  ||
Db       1331 TCGTTAGTCGATATGATTGATACGCTCAAGTCTGAATGCATCGACACTACTCTCCTGGGG 1390

Qy       1381 TCCTTTCTAGAGAATCAAGATAATCCGCGATTCCCTAGCTACACTTCTGATGAGTCTTTA 1440
              ||||||||||||||||  ||||||||||||||||||||||||||||||||||||||||||||
Db       1391 TCCTTTCTAGAGAATCAGGATAATCCGCGATTCCCTAGCTACACTTCTGATGAGTCTTTA 1450

Qy       1441 ATTAAAAATGCGATCGCTTTCACTATGCTCTCAGACGGCATTCCCATAATTTATTACGGT 1500
              ||||||||||||||  ||||||||||  ||||||||||||||||||||  ||||||||
Db       1451 ATTAAAAATGCGATTGCTTTCACTATACTCTCAGACGGCATTCCCATAATATATTACGGC 1510

Qy       1501 CAGGAGCAAGGCCTCAATGGTGGAAACGATCCCTATAATCGAGAGGCGCTTTGGCTTACG 1560
              ||  ||||||||  ||||||||||||||  ||||||||||||||||||||||||||||  |||
Db       1511 CAAGAGCAAGGACTCAATGGTGGAAATGATCCCTATAATCGAGAGGCGCTTTGGCCTACA 1570

Qy       1561 GGCTACTCCACAACGTCGACGTTCTACAAATACATTGCGTCGTTGAATCAGATTAGAAAT 1620
              |||||  ||||||||  ||  |||||  |||  |||||||  ||||||  ||||||||||  ||||||
Db       1571 GGCTATTCCACAACCTCAACGTTTTACGAATACATCGCGTCGCTGAATCAGATCAGAAAT 1630

Qy       1621 CAGGCTATATACAAAGATGATACTTATCTCACATATCAGAACTGGGTTATTTATTCGGAT 1680
              ||  ||||||||||  ||||||||||||||  ||||||||||  ||||||||||||||||||
Db       1631 CATGCTATATACATAGATGATACTTATCTTACATATCAGAATTGGGTTATTTATTCGGAT 1690

Qy       1681 TCCACGACAATAGCAATGCGGAAAGGTTTTACAGGGAACCAAATAATTACGGTTCTGTCA 1740
              ||||||||  ||||||||||||||||  |||||  ||||||||||  |||||  |||||  |||
Db       1691 TCCACGACTATAGCAATGCGGAAAGGATTTACGGGGAACCAAATCATTACTGTTCTATCA 1750

Qy       1741 AATCTTGGGACCAGTGGCAGTTCGTACACTTTGACGCTTTCGAATACGGGATATACCGCA 1800
              |||||||||  ||||||||||||||||||||||||||||  ||||||||||||||  |||
Db       1751 AATCTTGGGTCCAGTGGCAGTTCGTACACTTTGACGCTTTCCAATACGGGATATACTGCA 1810
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Qy       1801 TCTAGCGTTGTATATGAGATCTTGACATGCACAGCTGTGACTGTGGATTCGTCTGGGAAT 1860
             |||||||||||||||||||||||||||||||||||||||| |||||||||| ||| || |||
Db       1811 TCTAGCGTTGTATATGAGATCTTGACATGCACAGCTGTCACTGTGGATTTGTCCGGAAAT 1870

Qy       1861 TTGGCAGTGCCGATGTCCAGTGGCCTACCAAAAGTCTTTTATCAGGAATCGCAACTGGTT 1920
             |||||||||||| |||||| ||||| |||| | ||| ||||| |  ||||||||||||||||
Db       1871 TTGGCAGTGCCAATGTCCGGTGGCTTACCGAGAGTGTTTTACCCCGAATCGCAACTGGTT 1930

Qy       1921 GGCTCTGGAATCTGCTCCATGTAGAG 1946
             |||||||||||||||||||||||||||
Db       1931 GGCTCTGGAATCTGCTCCATGTAGAG 1956
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The said LKA1 gene (Accession U30376) encoding the reference α-amylase of Styen et al. is deemed to be a "derivative" of the claimed gene of SEQ ID NO: 2 since it has a high nucleotide sequence identity to SEQ ID NO: 2 of the instant application, and encodes the reference α-amylase which inherently has the same activity as the claimed protein, such as having dextranase activity, amylase activity, and hydrolyzing amylopectin, starch, glycogen, and amylase.

Styen et al. teach transformed cells, such as transformed *Escherichia coli* DH5α cells (prokaryotic) and transformed *Saccharomyces cerevisiae* YPH259[pAJC2] cells (eukaryotic) expressing the said LKA1 gene (see entire reference publication, especially page 66, right column, section titled **(a) Cloning of the *LKA1* gene** to page 67, left column, line 10, in particular).

Styen et al. teach a method for producing the reference α-amylase which inherently has the same activity of hydrolyzing amylopectin, starch, glycogen, and amylase as the claimed protein, comprising: culturing the transformed *Saccharomyces cerevisiae* YPH259[pAJC2] cells, expressing the reference α-amylase in the cultured *Saccharomyces cerevisiae* YPH259[pAJC2] cells, the cultured *Saccharomyces cerevisiae* YPH259[pAJC2] cells are mechanically disrupted by vortexing and centrifuged, and the culture supernatant containing the purified reference α-amylase removed for enzyme assay, where the supernatant is a composition comprising the reference α-amylase (see entire reference publication, especially page 69, left column, section titled **(d) Expression of *Sc* of *LKA1* and secretion of LKA1** to page 70, left

column, line 8; and Fig. 5, in particular). The reference enzyme is in a composition. Claims 8-10 are also included in the rejection because a composition is a composition, irrespective of its intended use. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Thus, the reference teachings of Styen et al. anticipate the claims.

Claim Rejections - 35 U.S.C. § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. (US Patent 6,485,953, published 11/26/2002) in view of Standing (Curr Opin Struct Biol. 2003

Oct;13(5):595-601; PTO 892) and Sambrook et al. (Molecular cloning A Laboratory Mannual, 2nd edition, Cold Spring Harbor, N.Y. 1989, pages 8.46-8.52 and pages 11.2-11.19; PTO 892). For the purpose of this art rejection, claim 2 has been interpreted as an isolated polynucleotide of SEQ ID NO: 2 which encodes a protein comprising an amino acid sequence of SEQ ID NO: 1.

The reference teachings of Kim et al. have been stated above. The teachings of Kim et al. differ from the claim in that Kim et al. does not teach an isolated polynucleotide of SEQ ID NO: 2 which encodes a protein comprising an amino acid sequence of SEQ ID NO: 1.

Standing teaches mass spectrometry methods to obtain the amino acid sequence of peptides and proteins, where *de novo* protein sequencing by mass spectrometry methods dates back more than 30 years (see entire publication, especially page 595, right column, second full paragraph to page 598, right column, last full paragraph).

Sambrook et al. teach widely known conventional methods to obtain and isolate the nucleic acid encoding a desired protein using the amino acid sequence of the desired protein to synthesize degenerate pools of oligonucleotide probes which are used to screen DNA libraries for the sought nucleic acid encoding the desired protein and recombinant protein expression and purification methods to obtain large amounts of recombinant proteins using expression vectors. See all volumes of Sambrook et al., especially pages 8.46-8.52 and pages 11.2-11.19.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the mass spectrometry methods taught by Standing to obtain the amino acid sequence of the DXAMase taught by Kim et al., and then use the obtained amino acid sequence of the DXAMase with the conventional methodologies taught by Sambrook et al. to thereby isolate the polynucleotide of SEQ ID NO: 2 encoding the DXAMase of Kim et al.

One of ordinary skill in the art at the time the invention was made would have been

motivated to do the above because Kim et al. teach the DXAMase is useful for plaque elimination and for the purpose of obtaining the isolated polynucleotide of SEQ ID NO: 2 encoding the DXAMase of Kim et al., which can be then cloned into expression vectors and used in recombinant protein expression and purification methods to easily obtain large amounts of purified DXAMase as taught by Sambrook et al..

One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for success because of the high level of skill in the art since *de novo* protein sequencing by mass spectrometry methods dates back more than 30 years as taught by Standing, and molecular biology techniques for making synthetic oligonucleotide probes and DNA library screening are widely known and available. For example, see all volumes of Sambrook et al. (Molecular cloning A Laboratory Mannual, 2nd edition, Cold Spring Harbor, N.Y. 1989), which is a comprehensive collection of well-known molecular biology techniques.

This rejection is based on the decision of *Ex parte* MAREK Z. KUBIN and RAYMOND G. GOODWIN (*Ex Parte Kubin & Goodwin*, No. 2007-0819, 2007 WL 2070495 (Bd.Pat.App. & Interf. May 31, 2007), where the board relied heavily on *KSR* (*KSR Int'l Co. v. Teleflex Inc.*, 550 U.S.-, 82 USPQ2d 1385, 1394, 1396 (2007).

In *Ex parte* MAREK Z. KUBIN and RAYMOND G. GOODWIN, the board found that the claimed nucleic acid encoding the NAIL protein to be obvious over a reference that discloses the NAIL protein and a reference teaching methodologies for isolating the corresponding encoding cDNA. Relying on *KSR,* the board found that:

> "Appellants heavily rely on *Deuel*. (*See, e.g.*, Br. 19.) To the extent *Deuel* is considered relevant to this case, we note the Supreme Court recently cast doubt on the viability of *Deuel* to the extent the Federal Circuit rejected an "obvious to try" test. *See KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, ___, 82 USPQ2d 1385, 1394, 1396 (2007) (citing *Deuel*, 51 F.3d at 1559). Under *KSR*, it's now apparent "obvious to try" may be an appropriate test in more situations than we previously contemplated.
> When there is motivation

> to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.

KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727, ___, 82 USPQ2d 1385, 1397 (2007). This reasoning is applicable here. The "problem" facing those in the art was to isolate NAIL cDNA, and there were a limited number of methodologies available to do so. The skilled artisan would have had reason to try these methodologies with the reasonable expectation that at least one would be successful. Thus, isolating NAIL cDNA was "the product not of innovation but of ordinary skill and common sense," leading us to conclude NAIL cDNA is not patentable as it would have been obvious to isolate it." (see pages 8-9).

Accordingly, isolating the polynucleotide of SEQ ID NO: 2 encoding a protein comprising an amino acid sequence of SEQ ID NO: 1 is concluded to be the product not of innovation but of ordinary skill and common sense, and therefore, the polynucleotide of SEQ ID NO: 2 is not patentable as it would have been obvious to isolate.

17. Claims 3, 4, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. (US Patent 6,485,953, published 11/26/2002) in view of Standing (Curr Opin Struct Biol. 2003 Oct;13(5):595-601; PTO 892) and Sambrook et al. (Molecular cloning A Laboratory Mannual, 2nd edition, Cold Spring Harbor, N.Y. 1989, pages 8.46-8.52 and pages 11.2-11.19; PTO 892) as applied to claim 2 above; and further in view of Guan et al. (US Patent 5,643,758, published 07/01/1997; PTO 892).

Guan et al. teach expression vectors containing nucleic acids encoding proteins such as beta-galactosidase fused to the *E.coli* maltose binding protein (MBP); isolated prokaryotic and eukaryotic host cells such as *E.coli* and yeast, respectively, transformed with said expression

vectors; culturing methods for making and expressing any protein fused to said *E.coli* MBP by culturing said host cells under conditions suitable for the protein's expression (such as culturing in rich media) and recovering the produced protein in large, highly-purified quantities from the host cell culture by centrifugation, sonication, and chromatography including affinity chromatography targeting the *E.coli* MBP; and Guan et al. teach that that these methods and products are useful for purifying any protein (see entire publication of US Patent 5,643,758, especially column 1, lines 11-25; column 4, line 49 to column 9, line 49; and Examples I-IV found on column 9, line 66 to column 20, line 40). Guan et al. teach the successful expression, isolation, and purification of beta-galactosidase (see EXAMPLE I), PstI restriction endonuclease (see EXAMPLE II), and paramyosin (see EXAMPLE IV).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to insert the obtained isolated polynucleotide of SEQ ID NO: 2 encoding the DXAMase of Kim et al. into the expression vector of Guan et al. and the modified expression vector transformed into prokaryotic or eukaryotic host cells such as the *E.coli* and yeast cells, respectively, of Guan et al. to thereby make a transformed prokaryotic or eukaryotic cell expressing the obtained isolated polynucleotide of SEQ ID NO: 2 encoding the DXAMase of Kim et al. fused to the *E.coli* MBP. Furthermore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the culturing method of Guan et al. such that the transformed prokaryotic or eukaryotic cell expressing the obtained isolated polynucleotide of SEQ ID NO: 2 encoding the DXAMase of Kim et al. fused to the *E.coli* MBP is cultured under conditions suitable for the expression of the DXAMase of Kim et al. and recovering the produced protein in large, highly-purified quantities from the host cell culture by centrifugation, sonication, and chromatography including affinity chromatography targeting the *E.coli* MBP.

One of ordinary skill in the art at the time the invention was made would have been motivated to do the above for the purpose of obtaining large, highly-purified quantities of the

DXAMase of Kim et al. from the host cell. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for success because Kim et al. teach DXAMase is useful for plaque removal, and Guan et al. teach that that these methods and products are useful for purifying any protein in large, purified quantities, and Guan et al. was successful in the expression, isolation, and purification of beta-galactosidase, PstI restriction endonuclease, and paramyosin.

Conclusion

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Thursday and alternate Fridays between 9:00AM - 6:30PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

20. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR

system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Christian L. Fronda/
Patent Examiner
Art Unit 1652